

### AMENDMENTS TO THE CLAIMS

Claim 1 (Withdrawn): A combination, comprising:

- a) an oxidizing agent or a reducing agent;
- b) a protein denaturing agent; and
- c) a hapten.

Claim 2 (Withdrawn): The combination of claim 1, wherein the oxidizing or reducing agent, the protein denaturing agent and the hapten are formulated in a single pharmaceutical composition or each is formulated in a separate pharmaceutical composition.

Claim 3 (Withdrawn): The combination of claim 1, wherein the oxidizing agent is selected from the group consisting of hydrogen peroxide ( $\text{H}_2\text{O}_2$ ), ozone ( $\text{O}_3$ ), polyatomic oxygen  $\text{O}_7$ , polyatomic oxygen  $\text{O}_8$ ,  $\text{NaIO}_4$ , potassium peroxymonosulfate (oxone), D,L-S-methylipoic acid methyl ester, tertiary butyl hydroperoxide, menadione, diamide, iodogen, N-bromosuccinimide, omeprazole and N-ethylmaleimide.

Claim 4 (Withdrawn): The combination of claim 1, wherein the reducing agent is selected from the group consisting of hematoxylin, a hypoxic reducing agent, and nonnitro compound tirapazamine (SR-4233).

Claim 5 (Withdrawn): The combination of claim 4, wherein the hypoxic reducing agent is a nitroimidazole.

Claim 6 (Withdrawn): The combination of claim 1, wherein the protein denaturing agent is selected from the group consisting of an alcohol, guanidine hydrochloride, guanidinium thiocyanate, sodium citrate, 2-mercaptoethanol, the ionic detergent sarcosyl, phenol, chloroform and urea.

Claim 7 (Withdrawn): The combination of claim 6, wherein the alcohol is selected from the group consisting of methyl, ethyl, *n*-propyl, *n*-butyl, *n*-pentyl, *n*-hexyl, *n*-heptyl, *n*-octyl, *n*-decyl, *n*-dodecyl, *n*-tetradecyl, *n*-hexadecyl, *n*-octadecyl, isopropyl, isobutyl, *sec*-butyl, *tert*-butyl, isopentyl, *active*-amyl, *tert*-pentyl, cyclopentanol, cyclohexanol, allyl, crotyl, methylvinylmethanol, benzyl,  $\alpha$ -phenylethyl,  $\beta$ -phenylethyl, diphenylmethanol, triphenylmethanol, cinnamyl, 1,2-ethanediol, 1,2-propanediol, 1,3-propanediol, glycerol and pentaerythritol alcohol.

Claim 8 (Withdrawn): The combination of claim 7, wherein the alcohol is ethanol.

Claim 9 (Withdrawn): The combination of claim 1, wherein the hapten is selected from the group consisting of trinitrophenol (TNP), dinitrophenol (DNP), N-iodoacetyl-N'-(5-sulfonic 1-naphthyl) ethylene diamine (AED), dinitrofluorobenzene(DNFB) and Ovabulin (OVA).

Claim 10 (Withdrawn): The combination of claim 1, further comprising an anti-neoplasm agent.

Claim 11 (Withdrawn): The combination of claim 10, wherein the anti-neoplasm agent is an anti-angiogenic agent.

Claim 12 (Withdrawn): The combination of claim 11, wherein the anti-angiogenic agent is selected from the group consisting of an inhibitor of basement membrane degradation, an inhibitor of cell migration, an inhibitor of endothelial cell proliferation, an inhibitor of three-dimensional organization and establishment of potency.

Claim 13 (Withdrawn): The combination of claim 11, wherein the anti-angiogenic agent is selected from the group consisting of an inhibitor of basement membrane degradation, an inhibitor of cell migration, an inhibitor of endothelial cell proliferation, an inhibitor of three-dimensional organization and establishment of potency. The combination of claim 11, wherein the anti-angiogenic agent is selected from the group consisting of an angiostatic gene, an angiostatic chemokine gene, AGM-1470 (TNP-470), angiostatic steroids, angiostatin, antibodies against  $\alpha v \beta 3$ ,

antibodies against bFGF, antibodies against IL-1, antibodies against TNF- $\alpha$ , antibodies against VEGF, auranofin, azathioprine, BB-94, BB-2516, basic FGF-soluble receptor, carboxyamido-trizole (CAI), cartilage-derived inhibitor (CDI), chitin, chloroquine, cisplatin, CM 101, cortisone/heparin, cortisone/hyaluroflan, cortexolone/heparin, CT-2584, cyclophosphamide, cyclosporin A, dexamethasone, diclofenac/hyaluronan, eosinophilic major basic protein, fibronectin peptides, gelatinase inhibitor, glioma-derived angiogenesis inhibitory factor (GD-AIF), GM 1474, gold chloride, gold thiomalate, heparinases, hyaluronan (high and low molecular-weight species), hydrocortisone/beta-cyclodextran, ibuprofen, indomethacin, interferon-alpha, interferon gamma-inducible protein 10, interferon-gamma, IL-1, IL-2, IL-4, IL-12, laminin, levamisole, linomide, LM609, matrix metalloproteinase inhibitor, marimastat (BB-2516), medroxyprogesterone, 6-methylmercaptapurine riboside, metastat (Col-3), methotrexate, minocycline, nitric oxide, octreotide (somatostatin analogue), Paclitaxel, D-penicillamine, pentosan polysulfate, placental proliferin-related protein, placental Rnase inhibitor, plasminogen activator inhibitor (PAIs), platelet factor-4 (PF4), prednisolone, prolactin (16-Kda fragment), proliferin-related protein, prostaglandin synthase inhibitor, protamine, retinoids, Roquinimex (LS-2616. linomide), somatostatin, stromelysin inhibitor, substance P, suramin, SU101, tecogalan sodium (DS-4152), tetrahydrocortisol-sthrombospondins (TSPs), tissue inhibitor of metalloproteinases (TIMP 1, 2, 3), vascular endothelial growth factor inhibitors, vitamin A, Vitaxin and vitreous fluids.

Claim 14 (Withdrawn): The combination of claim 10, wherein the anti-neoplasm agent is selected from the group consisting of an alkylating agent, an antimetabolite, a natural product, a platinum coordination complex, an anthracenedione, a substituted urea, a methylhydrazine derivative, an adrenocortical suppressant, a hormone, an antagonist, an anti-cancer polysaccharide and an anti-cancer herb extract.

Claim 15 (Withdrawn): The combination of claim 10, wherein the anti-neoplasm agent is an oncogene inhibitor or a tumor suppressor gene or protein.

Claim 16 (Withdrawn): The combination of claim 15, wherein the oncogene inhibitor is an anti-oncogene antibody or an anti-oncogene antisense oligonucleotide.

Claim 17 (Withdrawn): The combination of claim 15, wherein the oncogene is selected from the group consisting of *abl*, *erbA*, *erbB*, *ets*, *fes* (*fps*), *fgr*, *fms*, *fos*, *hst*, *int1*, *int2*, *jun*, *hit*, *B-lym*, *mas*, *met*, *mil* (*raf*), *mos*, *myb*, *myc*, *N-myc*, *neu* (*ErbB2*), *ral* (*mil*), *Ha-ras*, *Ki-ras*, *N-ras*, *rel*, *ros*, *sis*, *src*, *ski*, *trk* and *yes*.

Claim 18 (Withdrawn): The combination of claim 15, wherein the tumor suppressor gene is selected from the group consisting of *p16*, *p21*, *p27*, *p53*, *RB*, *WT-1*, *DCC*, *NF-1* and *APC*.

Claim 19 (Withdrawn): The combination of claim 1, further comprising a viral vector carrying an oncogene or a tumor suppressor gene sequence.

Claim 20 (Withdrawn): The combination of claim 19, wherein the viral vector is selected from the group consisting of an adenovirus vector, a simian virus vector, a conditionally replicating human immunodeficiency viral vector, a retrovirus vector, a SV40 vector, a Herpes simplex viral amplicon vector and a Vaccinia virus vector.

Claim 21 (Withdrawn): The combination of claim 1, further comprising a facilitating agent that facilitates conjugation between the hapten and a tumor antigen.

Claim 22 (Withdrawn): The combination of claim 21, wherein the facilitating agent is a chelator or a chemical linking agent.

Claim 23 (Withdrawn): The combination of claim 22, wherein the chelator is glycytyrosyl-(N-e-diethylenetri-aminepetaacetic acid)-lysine (GYK-DTPA) or doxorubicin adipic-dihydrazide (ADR-ADH).

Claim 24 (Withdrawn): The combination of claim 22, wherein the chemical linking agent is carbodiimide.

Claim 25 (Withdrawn): The combination of claim 1, further comprising an immune response potentiator.

Claim 26 (Withdrawn): The combination of claim 25, wherein the immune response potentiator is selected from the group consisting of Bacille Calmette-Guerin (BCG), Corynebacterium Parvum, Brucella abortus extract, glucan, levamisole, tilorone, an enzyme and a non-virulent virus.

Claim 27 (Withdrawn): The combination of claim 26, wherein the enzyme is selected from the group consisting of Vibrio cholera neuraminidase (VCN), Papain,  $\beta$ -Gal and ConA.

Claim 28 (Withdrawn): The combination of claim 26, wherein the non-virulent virus is a non-virulent Newcastle virus.

Claim 29 (Withdrawn): The combination of claim 1, further comprising a coagulation lysing agent.

Claim 30 (Withdrawn): The combination of claim 29, wherein the coagulation lysing agent is selected from the group consisting of proteinase K, Glycosyl-phosphatidylinositol-B7 and pancreatin.

Claim 31 (Withdrawn): The combination of claim 1, wherein the oxidizing agent is  $H_2O_2$ , the protein denaturing agent is ethanol and the hapten is TNP.

Claim 32 (Withdrawn): The combination of claim 21, wherein the oxidizing agent is  $H_2O_2$ , the protein denaturing agent is ethanol, the hapten is TNP and the facilitating agent is carbodiimide.

Claim 33 (Withdrawn): The combination of claim 1, wherein the oxidizing agent or reducing agent is from about 0.01% (w/w) to about 35% (w/w), the protein denaturing agent is from about 1% (w/w) to about 99% (w/w) and the hapten is from about 1 mg/ml to about 80 mg/ml.

Claim 34 (Withdrawn): A kit, comprising the combination of claim 1.

Claim 35 (Withdrawn): An article of manufacture, comprising:

- a) packaging material;
- b) the combination of claim 1; and
- c) a label indicating that the article is for treating neoplasms.

Claim 36 (Previously Presented): A method for treating neoplasm in a mammal, comprising *in situ* administering to neoplasm of a mammal an effective amount of a hapten and coagulation agent(s) that causes coagulation of the neoplasm, wherein said hapten is trinitrophenol (TNP) and said coagulation agents are a combination of H<sub>2</sub>O<sub>2</sub> and ethanol, whereby an immune response is generated against the neoplasm and the neoplasm is treated.

Claim 37 (Original): The method of claim 36, wherein the mammal is a human.

Claim 38 (Cancelled)

Claim 39 (Original): The method of claim 36, further comprising administering to neoplasm a facilitating agent that facilitates conjugation between the hapten and a tumor antigen of the neoplasm.

Claim 40 (Original): The method of claim 39, wherein the facilitating agent is a chelator or a chemical linking agent.

Claim 41 (Cancelled)

Claim 42 (Original): The method of claim 40, wherein the chemical linking agent is carbodiimide.

Claim 43 (Original): The method of claim 36, further comprising administering an immune response potentiator to the neoplasm.

Claim 44 (Currently Amended): The method of claim 43, wherein the immune response potentiator is selected from the group consisting of Bacille Calmette-Guerin (BCG), Corynebacterium Parvum, Brucella abortus extract, glucan, levamisole, tilorone, an enzyme selected from the group consisting of Vibrio cholera neuraminidase (VCN), Papain,  $\beta$ -Gal and ConA, a non-virulent Newcastle virus, and a polysaccharide selected from the group consisting of glucomannan,  $\beta$ -(1-->3)-D-linked glucose, sizofiran (SPG), schizophyllan, mannan, lentinan, Su-polysaccharide (Su-Ps) and mannozym and a herb extract.

Claim 45 (Withdrawn): The method of claim 44, wherein the enzyme is selected from the group consisting of Vibrio cholera neuraminidase (VCN), Papain,  $\beta$ -Gal and ConA.

Claim 46 (Withdrawn): The method of claim 44, wherein the non-virulent virus is a non-virulent Newcastle virus.

Claim 47 (Original): The method of claim 36, further comprising administering a coagulation lysing agent to the neoplasm.

Claim 48 (Original): The method of claim 47, wherein the coagulation lysing agent is selected from the group consisting of proteinase K, Glycosyl-phosphatidylinositol-B7 and pancreatin.

Claim 49 (Cancelled)

Claim 50 (Previously Presented): The method of claim 36, wherein the TNP, H<sub>2</sub>O<sub>2</sub> and ethanol are formulated in a single pharmaceutical composition or each is formulated in a separate pharmaceutical composition.

Claim 51 (Cancelled)

Claim 52 (Cancelled)

Claim 53 (Currently Amended): The method of claim ~~52~~ 36, ~~wherein the hypoxie reducing agent is~~ further comprising administering a nitroimidazole.

Claim 54 (Cancelled)

Claim 55 (Cancelled)

Claim 56 (Cancelled)

Claim 57 (Currently Amended): The method of claim ~~49~~ 36, further comprising administering AraC to the mammal.

Claim 58 (Cancelled)

Claim 59 (Cancelled)

Claim 60 (Cancelled)

Claim 61 (Cancelled)

Claim 62 (Cancelled)

Claim 63 (Cancelled)



Claim 64 (Cancelled)

Claim 65 (Cancelled)

Claim 66 (Cancelled)

Claim 67 (Cancelled)

Claim 68 (Cancelled)

Claim 69 (Previously Presented): The method of claim 36, wherein the H<sub>2</sub>O<sub>2</sub> is from about 0.01% (w/w) to about 35% (w/w), the ethanol is from about 1% (w/w) to about 99% (w/w) and the TNP is from about 1 mg/ml to about 80 mg/ml.

Claim 70 (Cancelled)

Claim 71 (Currently Amended): The method of claim 36, wherein the autologous immune response generated by the combined action of the hapten and the coagulation agent ~~or treatment~~ comprises or is a humoral and/or cellular immune response.

Claim 72 (Currently Amended): The method of claim 36, wherein the neoplasm to be treated is selected from the group consisting of adrenal gland, anus, ~~auditory nerve~~, bile ducts, bladder, bone, brain, breast, ~~bruceal~~ buccal, ~~central nervous system~~, cervix, colon, ear, endometrium, esophagus, ~~eye~~, eyelids, fallopian tube, gastrointestinal tract, head and neck, heart, kidney, larynx, liver, lung, mandible, mandibular condyle, maxilla, mouth, nasopharynx, nose, oral cavity, ovary, pancreas, parotid gland, penis, pinna, pituitary, prostate gland, rectum, retina, salivary glands, skin, small intestine, ~~spinal cord~~, stomach, testes, thyroid, tonsil, urethra, uterus, vagina, ~~vestibulocochlear nerve~~ and vulva neoplasm.

Claim 73 (Original): The method of claim 36, wherein the neoplasm to be treated is a solid tumor.

Claim 74 (Original): The method of claim 73, wherein the size of the solid tumor is larger than  $10^8$  cells.

Claim 75 (Original): The method of claim 74, wherein the size of the solid tumor is from about  $5 \times 10^9$  to about  $10^{11}$  cells.

Claim 76 (Original): The method of claim 36, wherein the hapten and the coagulation agent(s) are administered to the neoplasm via injection.

Claim 77 (Original): The method of claim 36, wherein the hapten and the coagulation agent(s) are administered to the neoplasm in combination with a surgical procedure.

Claim 78 (Withdrawn): The combination of claim 1, further comprising a molecule selected from the group consisting of a suicide gene sequence, a cytolytic gene sequence, a cytokine gene sequence, a radiation sensitizer, a cytokine-containing depot, a reporter and a reporter gene sequence.

Claim 79 (Currently Amended): The method of claim 36, further comprising *in situ* administering ~~a molecule selected from the group consisting of a suicide gene sequence, a cytolytic gene sequence, a cytokine gene sequence, a radiation sensitizer, a cytokine-containing depot, a reporter and a reporter gene sequence.~~